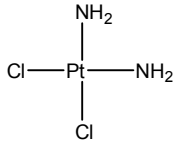
CISPLATIN
CAS No. 15663-27-1
First Listed in the *Fifth Annual Report on Carcinogens*



CARCINOGENICITY

Cisplatin is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals. When administered as multiple intraperitoneal injections, cisplatin significantly increased the incidence and number of lung adenomas in female mice. Similar treatments caused a significant increase in the incidence of skin papillomas in female mice given promoting treatment of croton oil applied to the skin. In two studies, when administered by multiple intraperitoneal injections, cisplatin induced leukemia in rats of both sexes (IARC V.26, 1981; IARC S.7, 1987).

There are no adequate data available to evaluate the carcinogenicity of cisplatin in humans. Occasional case reports of exposure to cisplatin, especially in the presence of concurrent therapy with other putative carcinogens, such as ionizing radiation, alkylating agents, and other potent oncotherapeutic drugs, do not constitute evidence of carcinogenesis. (IARC V.26, 1981; IARC S.7, 1987).

PROPERTIES

Cisplatin is a yellow crystalline solid that is slightly soluble in cold water and insoluble in most common solvents except *N,N*-dimethylformamide. In aqueous solution, cisplatin slowly changes to the trans form. It decomposes at approximately 270 ^{o}C. When heated to decomposition, cisplatin emits very toxic fumes of chlorine and nitrogen oxides (NO_x).

USE

Cisplatin is an experimental carcinogen (Sax and Lewis, 1987). It is used for the treatment of various malignancies, often in combination with other antineoplastic agents (Goodman and Gilman, 1980; IARC V.26, 1981). Since the 1970s cisplatin has been used in the treatment of testicular tumors; malignant melanoma; osteogenic sarcoma; carcinomas of the urinary bladder, lung (other than small cell), uterine cervix, and ovary; and squamous carcinoma of the head and neck region (IARC V.26, 1981).

PRODUCTION

Preparation of cisplatin was reported in the 1840s (IARC V.26, 1981). There has been at least one producer of cisplatin since 1986 (SRIa, 1997; USITC, 1989-1991, 1993-1995). Production volumes, however, have not been disclosed. *Chemcyclopedia 98* and the 1998

Chemical Buyers Directory identify three and six domestic suppliers of the chemical, respectively (Rodnan, 1997; Tilton, 1997).

EXPOSURE

The National Occupational Exposure Survey (1981-1983) estimates that 21,217 total workers, including 15,288 women, potentially were exposed to cisplatin (NIOSH, 1984). The ACGIH recommends a threshold limit value (TLV) for an 8-hr time-weighted average (TWA) of 0.002 mg/m^3 as platinum for soluble platinum salts (ACGIH, 1986). Short-term exposures may exceed three times the TLV-TWA for no more than a total of 30 minutes during a workday and under no circumstances should the short-term exposure exceed five times the TLV-TWA, provided that the TLV-TWA for 8 hours is not exceeded.

Cisplatin is a relatively new anticancer agent used in human medicine to treat a variety of malignancies (Searle, 1984). Since the compound is packaged as a powder, not only are patients exposed, but potential exposure exists for medical and pharmacy personnel, the pharmaceutical manufacturers, and hospital and clinic housekeeping personnel via skin absorption during production or inhalation during preparation of dosage forms (IARC V.26, 1981; HSDB, 1997).

REGULATIONS

OSHA regulates cisplatin under the Hazard Communication Standard and as a chemical hazard in laboratories. A PEL of 0.002 mg/m^3 (as platinum) has been established. Regulations are summarized in Volume II, Table B-29.